

# **Heartburn on PPIs: What test should I do now?**

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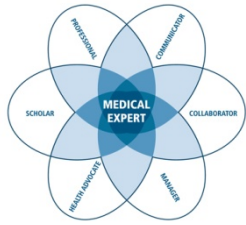
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# **Financial Interest Disclosure**

(over the past 24 months)

No relevant financial relationships with  
any commercial interests



## CDDW/CASL Meeting Session

### CanMEDS Roles Covered in this Session:

✓	<p><b>Medical Expert</b> (as <i>Medical Experts</i>, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional attitudes in their provision of patient-centered care. <i>Medical Expert</i> is the central physician Role in the CanMEDS framework.)</p>
	<p><b>Communicator</b> (as <i>Communicators</i>, physicians effectively facilitate the doctor-patient relationship and the dynamic exchanges that occur before, during, and after the medical encounter.)</p>
	<p><b>Collaborator</b> (as <i>Collaborators</i>, physicians effectively work within a healthcare team to achieve optimal patient care.)</p>
	<p><b>Manager</b> (as <i>Managers</i>, physicians are integral participants in healthcare organizations, organizing sustainable practices, making decisions about allocating resources, and contributing to the effectiveness of the healthcare system.)</p>
✓	<p><b>Health Advocate</b> (as <i>Health Advocates</i>, physicians responsibly use their expertise and influence to advance the health and well-being of individual patients, communities, and populations.)</p>
✓	<p><b>Scholar</b> (as <i>Scholars</i>, physicians demonstrate a lifelong commitment to reflective learning, as well as the creation, dissemination, application and translation of medical knowledge.)</p>
	<p><b>Professional</b> (as <i>Professionals</i>, physicians are committed to the health and well-being of individuals and society through ethical practice, profession-led regulation, and high personal standards of behaviour.)</p>

# Objectives

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At the end of this session participants should:

- Be aware of factors that might contribute to refractoriness to PPI therapy in reflux patients.
- Understand the pathophysiology of non-acid reflux related heartburn.
- Appreciate the role of ambulatory pH and impedance testing in the management of patients with ‘refractory’ heartburn.
- Know when ambulatory pH and/or impedance testing should be performed on versus off PPI therapy.

# Case Presentation

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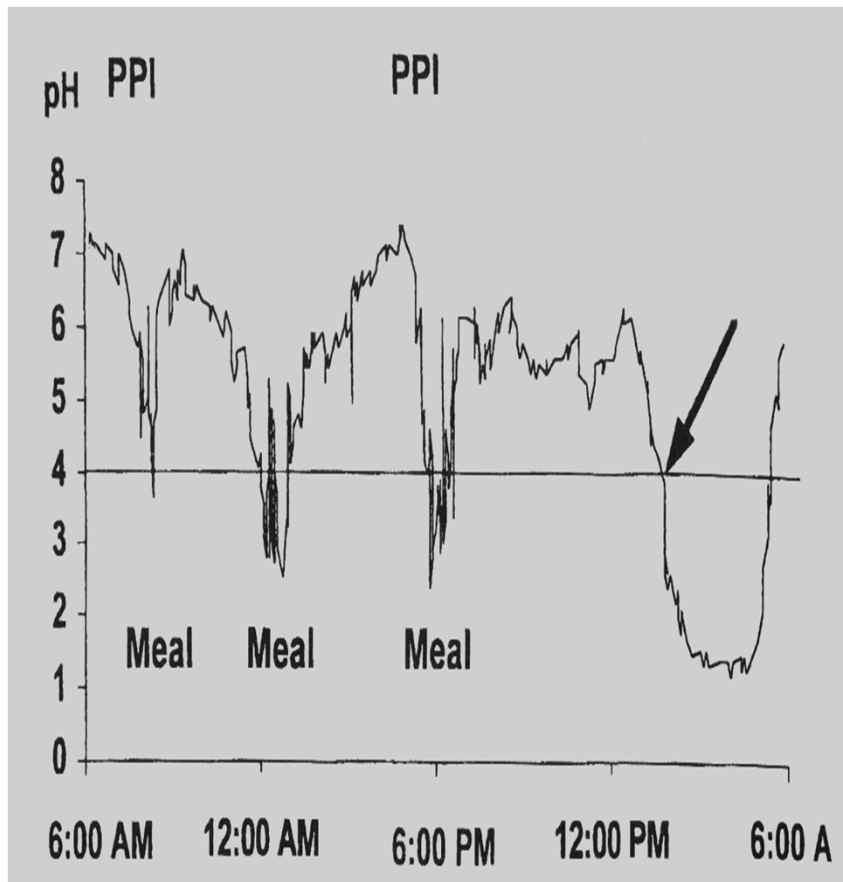
- 47 yo female is referred with a 10 year history of “heartburn” that has been worse over the last 2 years
- Describes burning discomfort that starts in high epigastric area, radiating to the upper sternum
- Heartburn present most of the time, but is worsened post-prandially and often awakens her from sleep.
- Occasional bitter taste in mouth, but no dysphagia, cough or laryngeal symptoms

## Case Presentation – cont' d

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- Symptoms have been marginally improved by bid/tid PPI therapy.
- Past history of inferior wall MI one year previously treated with stenting - dyslipidemia, 25 pack year smoker
- on clopidogrel, ASA, atorvastatin, metoprolol
- O/E normal – wt 59 kg
  
- What would you do?

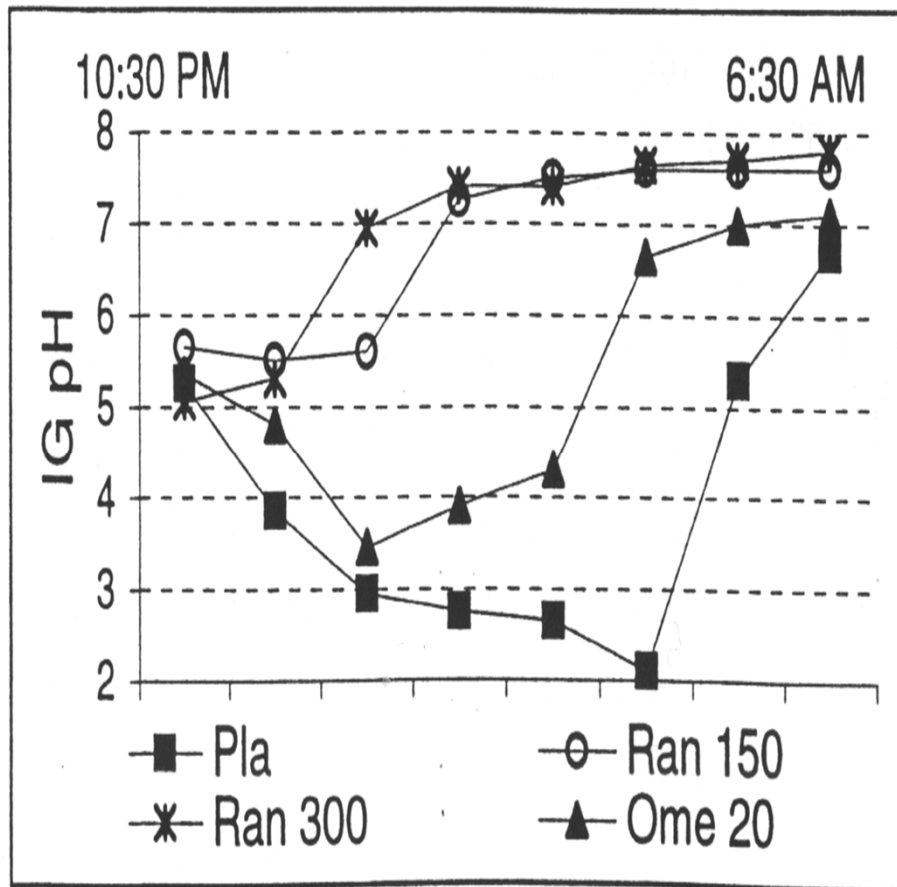
# Nocturnal recovery of gastric acid secretion with twice daily dosing of Proton Pump Inhibitors - Peghini et al Am. J. Gastro. 1999



- “Acid breakthrough” (recovery of nocturnal acid secretion > 1 hr) occurred in 75% of patients and volunteers on bid omeprazole or lansoprazole
- Median time to breakthrough = 7.5 h from last dose

# Ranitidine controls nocturnal gastric acid breakthrough on Omeprazole

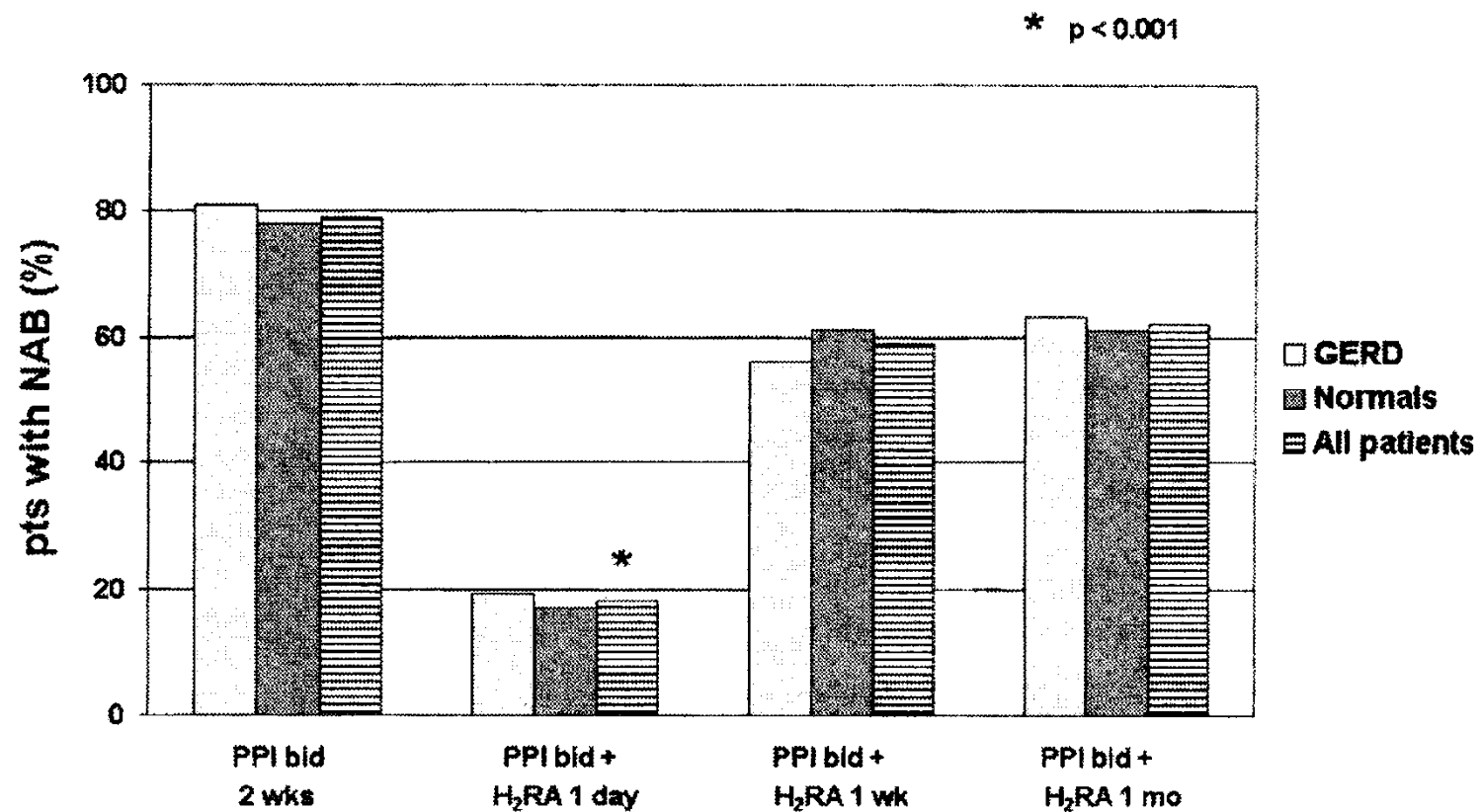
Peghini et al, Gastroenterology 1999 -



- When added to a twice daily dose of omeprazole, ranitidine (150 mg or 300 mg) at bedtime was more efficacious than a third dose of omeprazole at bedtime in suppressing nocturnal gastric acid secretion.



# Benefit of nocturnal H2RA is not sustained



Fackler et al. Gastro 2002

# Role of Endoscopy in PPI refractory heartburn (from Sifrim & Zerbib Gut 2012)

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- *Diagnose erosive esophagitis or Barrett's* ( but only 6.7% have erosive disease on once daily PPI and this includes patients with an incomplete response to PPI\*)
- *Exclude EoE* - (but this would be a rare finding in patients with refractory heartburn with no dysphagia)
- *Suspect pill-induced esophagitis or esophagitis secondary to skin diseases*

\* Poh et al. Gastrointest Endoscopy 2010

# Ambulatory pH monitoring in patients with refractory heartburn (ACG Guidelines AJG 2007)

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## *“pH testing is useful”:*

- Evaluation of endoscopy-negative patients with typical reflux symptoms that are refractory to PPI therapy.
- pH study done on-therapy, but consider extended testing with wireless pH system incorporating periods of both off- and on-therapy. The diagnostic yield of on-therapy testing in patients who have not symptomatically responded to b.i.d. PPI therapy is limited.
- Use of a symptom correlation measure (SI, SSI, or SAP) is recommended to statistically interpret the causality of a specific symptom with episodes of acid reflux. These statistical measures, however, do not ensure a response to antireflux therapy

# Ambulatory pH monitoring in patients with refractory heartburn (ACG Guidelines AJG 2007)

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*“pH monitoring may be useful”:*

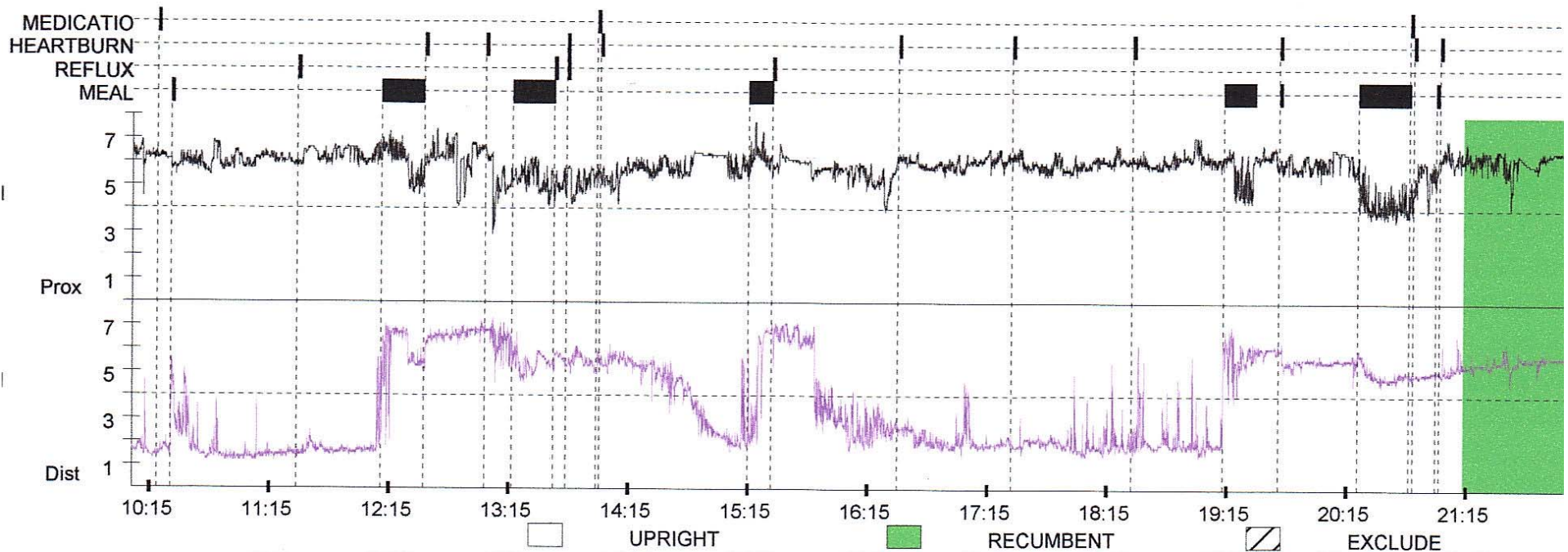
- Evaluation of endoscopy-negative patients with atypical reflux symptoms that are refractory to b.i.d. PPI therapy.
- The diagnostic yield of pH testing under such circumstances is low.
- pH study done on bid PPI therapy in patients with high pretest probability of GERD or off therapy in patients with low pretest probability of GERD. Pretest probability is based on prevalence of GERD in patient population under question, clinician's impression, and degree of response to empiric PPI trial.

## Case Presentation – cont' d

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- EGD performed - normal.
- 24 hr pH study done on therapy - pH<4 in esophagus for only 0.6% of recording period; gastric pH<4 for 54.4% of recording period

# Case Presentation – cont'd



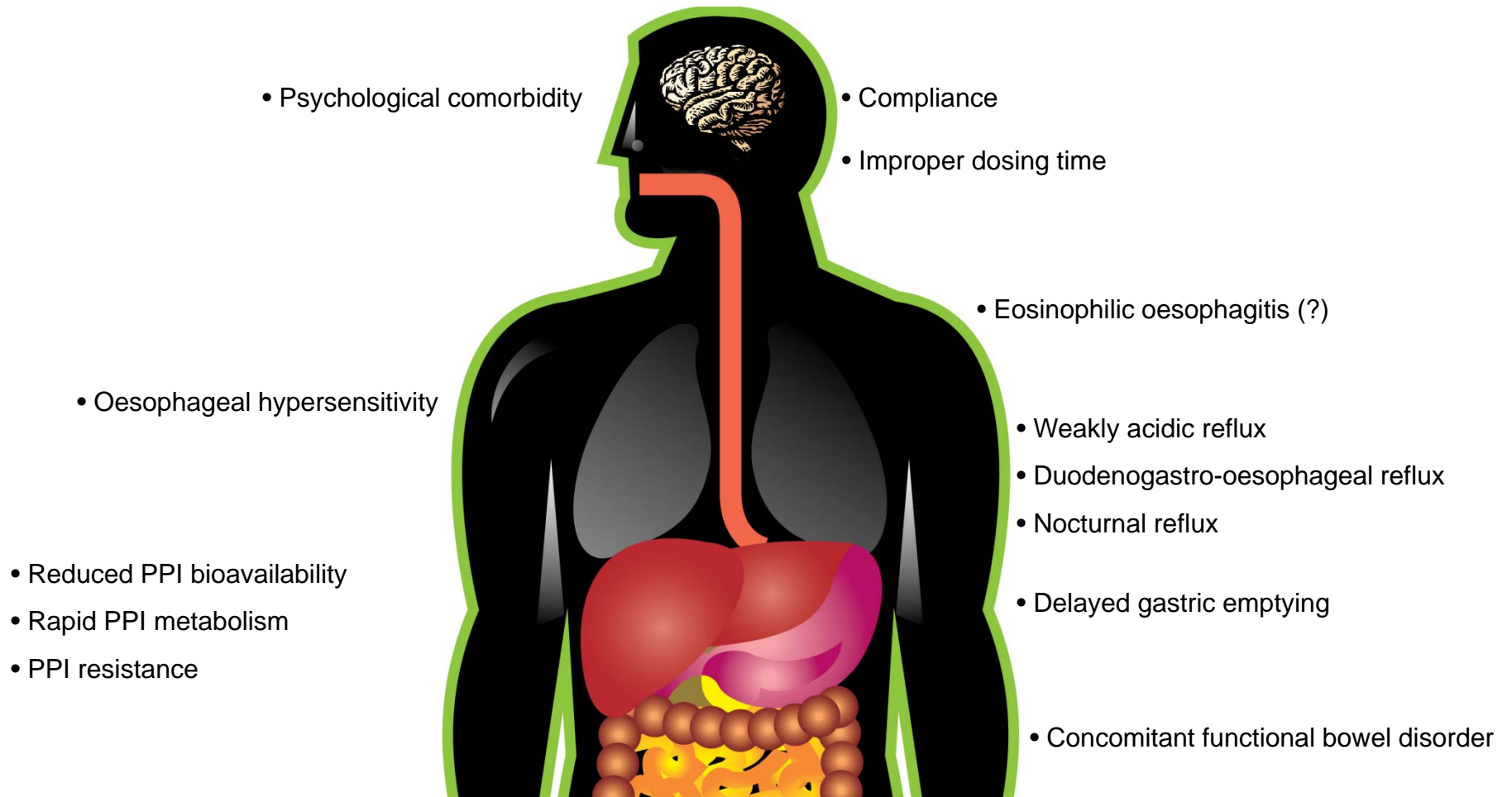
0 of 6 “reflux” episodes and 1 of 13 “heartburn” episodes correlated temporally with acid reflux events

- What is your diagnosis?
- Would ambulatory pH/impedance testing be useful in this patient?
- How would you manage the patient?

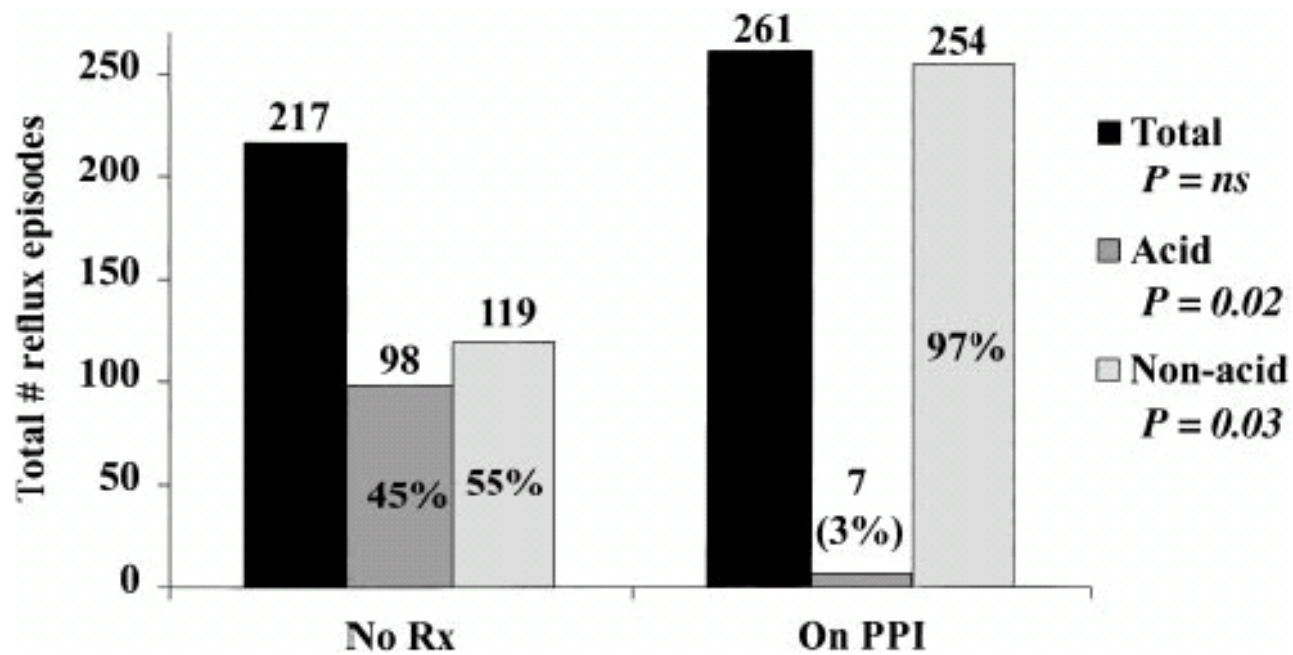
# Does this patient have GERD?

- Montreal definition
- Reflux of stomach contents into the esophagus causes symptoms and/or complications





# PPIs only change the acidity of refluxate



# 24hr pH study

- Can answer 2 questions
  1. Does this patient have GERD?
    - test performed with pt OFF PPI
  2. In a patient with GERD, is the acid suppression working?
    - may reflect compliance, drug interactions, PPI hypermetabolizers, etc (test performed on PPI)

# 24hr pH-impedance study

- Can answer several questions
- Does this patient have GERD?
- Are this patient's symptoms due to acid reflux?
  - can be physiologic (pt has visceral hypersensitivity) or pathologic (pt has GERD)
- Are this patient's symptoms due to non-acid reflux?
- How high into the esophagus does the reflux reach?

# Which test to use?

- 24hr pH-impedance overall gives more information
- OFF PPI – suspect that this is not actually GERD
- ON PPI – non-acid reflux, extra-esophageal symptoms, save pt. a second test

# ROME III criteria: Functional GERD

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Presence for at least 3 months, with onset at least 6 months before diagnosis of:

1. Burning retro-sternal discomfort or pain; and
2. Absence of evidence that gastro-esophageal acid reflux is the cause of symptoms; and
3. Absence of histopathology based esophageal motility disorders

# Functional Heartburn: Pathogenesis

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- Pathogenesis unknown, but considered to be a disturbance in visceral perception (allodynia and/or hyperalgesia)
  - ? Initial inflammatory stimulus sensitizes esophageal afferents
  - Increased epithelial spacing (seen in NERD/GERD) facilitates activation of nociceptive receptors
  - ? Abnormal cortico-cerebral processing of esophageal signalling

# Functional Heartburn: Treatment

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- *Pain modulating drugs*
  - Low dose TCA<sup>1</sup>, SSRI's<sup>2</sup> or SARI<sup>3</sup> (desipramine, amitriptyline, citalopram, trazadone)
  
- *Relaxation therapy*<sup>4</sup>

1. Peghini, Gut 1998 2. Viazis et al., AJG 2012 3. Clouse et al., Gastro 1998. 4. McDonald-Haile, J et al., Gastro 1994.